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Sarcoidosis

Sarcoidosis was so named in 1899 by Boeck, a Norwegian dermatologist, who described nodular skin lesions which showed an epithelioid cell structure and which he believed to resemble sarcoma cells; hence the designation "sarcoid." Since that time many investigators have contributed to the knowledge of this disease but major credit for emphasizing its generalized nature goes to Schaumann. In a number of articles he correlated the clinical and pathologic features and emphasized that the disease was a disseminated condition of the lymphatic and hemopoietic systems. Further investigation has revealed that there may be widespread involvement of practically every organ in the body. The purpose of this article is to report the authors' observations of the clinical features and pathology of sarcoidosis based on their study of 24 cases observed at the Kennedy Veterans Hospital. While the series is not a large one, it differs from many others in that it does not represent a review of cases seen by a number of individuals, but includes only patients actually observed by the present writers over a period of nearly 5 years.

The basic lesion in sarcoidosis is the epithelioid granuloma. This is usually discrete and involves the lymphoreticular tissues, but any organ of the body may be the site of lesions. The pattern is often described as monotonous because the granulomas have a tendency to occur in "crops" showing the same stage of development. The lesions tend to remain discrete until the outline is blurred by fibrosis and hyalinization in the healing stage. This fibrotic healing begins after the earliest cellular lesion and at first encircles the granuloma with a thin layer of fibroblasts. The fibrous tissue develops into a compact layer which hyalinizes and finally forms a dense scar. Necrosis is not commonly a part of the lesion but a fibrinoid type of necrosis is encountered in some of the granulomas. This type of necrosis was observed either in biopsy or autopsy material in 7 of the 22 cases with tissue sections (32 %). The number of giant cells in the lesions is usually less than in tuberculosis, and both Langhans and foreign body type cells are encountered. Inclusions of Schaumann bodies and asteroid inclusions within the giant cells or free in the lesions are seen in some cases. Inclusion bodies or asteroid inclusions were present in 3 of the cases (14 %). In older lesions a hyalin material similar in appearance to amyloid is present but it does not take specific stains for amyloid. This has been termed para-amyloid by some writers, notably Teilum, who considers it a product of the elevated globulin level present in this condition.

It should be noted that granulomas similar to the cellular sarcoid granuloma may be seen in a variety of other conditions, notably in lymph nodes associated with regional ileitis, chronic gallbladder disease and even in Hodgkin's disease. These, plus the granulomas seen in lesions produced by beryllium, histoplasma and medicated oils, are designated "sarcoid lesions" as distinguished from the generalized disease "sarcoidosis."

The autopsied cases of sarcoidosis have been reviewed by Pinner who collected 43 cases. By 1950 the total number was brought to 99 cases, to which the present authors add 3 of their own.

Sarcoidosis is no longer to be considered rare. It is more common in the Negro than in the white patient and is manifested by a variety of clinical expressions. Most common involvement is of the lungs and lymph nodes although the eyes, skin, bones, liver and spleen are frequently affected. The authors emphasize the occurrence of rheumatic complaints and nervous system involvement. The prognosis is not as benign as has been thought generally. Three patients of their 24 died as a direct result of their disease. No form of treatment has proved of consistent value. (Am. J. Med., Feb. 1952, B. R. Gendel, J. M. Young & D. J. Greiner)

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The Physiology of Asphyxia

Normal respiration. We are surrounded by an atmosphere which consists of various gases and a certain amount of water vapor. Oxygen is present in about 21 % of the atmosphere; thus, the barometric pressure, when corrected for water vapor present, is due to oxygen. When we respire we draw a certain amount of gas into the lungs, where other gas is also present. Therefore the oxygen in the inspired air is somewhat diluted. In concentration, i.e., in percentage or in pressure of the atmosphere, the oxygen amounts to about two-thirds of the concentration or pressure present in the inspired air.

All of the air taken in at a single inspiration does not reach the depths of the lungs; about one-third of it is present in the air passages in the bronchi, trachea and bronchioles and therefore is not available for interchange with the blood. This is important in that whenever respiration becomes very shallow, less of the air drawn in reaches the depths of the lungs; less is available for the interchange of blood and the oxygen pressure in the pulmonary air decreases. Conversely, when we breathe more deeply, the oxygen pressure in the pulmonary air more nearly approaches that of the inspired air.

This oxygen pressure in the lungs supplies the head of pressure or the driving force which pushes oxygen across the pulmonary membrane and into the blood where it forms a reversible combination with the hemoglobin of the blood then being carried by the pumping action of the heart to the tissues. Oxygen is forced by the process of diffusion into the tissues because the oxygen pressure is higher in the blood than in the tissues. Conversely, carbon dioxide, being present under a higher head of pressure in the tissues than in the blood because it is formed by respiration of the cells, passes out into the blood. The CO_2 is then brought back through the lungs, where it is expelled.

Hypoxia. The anoxic form of oxygen lack is more commonly known as the hypoxic form. This primary defect is a decrease in the oxygen pressure and in the oxygen content of the arterial blood. The classic example is that of ascending into the atmosphere, either in an aircraft or when climbing a mountain. Under these circumstances, the surrounding atmosphere is present at a lower pressure, the decrease in barometric pressure being proportional to the increase

in altitude. The actual percentage of the various gases in the air under these circumstances does not change, but since the barometric pressure changes, there is a decrease in the partial pressure of oxygen present in the inspired air and therefore in the air in the depths of the lungs. The body attempts to compensate by increasing the rate and depth of respiration. Drawing more of the inspired air into the depths of the lungs increases the oxygen pressure in the pulmonary air, but this compensatory increase, while very important at high altitudes, is not great enough to be complete. Since the oxygen of the blood is in equilibrium with the oxygen in the pulmonary air, there is a decrease in the oxygen content and in the oxygen pressure in the blood. The blood is then brought to the tissues which are compelled to work under conditions of a decrease in oxygen content and in oxygen pressure.

Some circulatory compensation takes place by an increase in cardiac output so that the blood flow is increased. The amount of blood, and therefore the amount of oxygen brought to the tissues, increases in the meantime. Other compensations occur in the kidney, increased activity of the red bone marrow and increased amount of red cells and therefore enhanced oxygen-carrying power of the blood. The increase in red cells occurs at high altitude over a period of some days and weeks.

Clinically, this type of anoxia may be present under any conditions which interfere with the oxygenation of the blood. For example, if the airway is occluded in any way as by a foreign body or presence of vomitus and edema of the larynx, or if there is any interference with the interchange of oxygen in the pulmonary epithelium (produced, for example, by the presence of vibrant exudate, fibrosis or pulmonary edema), there is interference with the interchange of oxygen, and the arterial blood is therefore decreased in content and in pressure.

Anoxia caused by decreased blood volume. Whenever the volume of blood present is decreased, as by loss of blood to the exterior as in hemorrhage, by a loss of large amounts of blood to the tissues as in tissue trauma or by the loss of large amounts of plasma as occurs in burns, a condition obtains in which there is a decrease in the flow of blood to the periphery. The blood volume, the venous inflow to the right heart, and the output of blood by the left heart are reduced, and the flow of oxygen to the tissues in a given time is therefore markedly reduced. For a given reduction in blood volume there is a decrease in the cardiac output which is proportionately very much greater. Thus, the normal man who loses 20 % of his blood volume is on the verge of circulatory collapse; if he loses 30-40 % of his blood volume, signs and symptoms, which are recognized clinically as secondary traumatic or surgical shock, ensue.

It is not generally realized what large amounts of blood may be lost into the tissues. One can calculate that an increase of only 1 cm. in the diameter of the thigh can be responsible for the presence of a liter of blood in the thigh. There are rather considerable losses of whole blood when fractures of the limbs occur. Three fractures of a limb or a fracture of the pelvis will result in a 30-40 % reduction in blood volume and the presence of secondary or traumatic shock. In cases of traumatic injury, the decrease in blood volume that takes place is equal to the increase in tissue volume in the injured region. Whereas hemodilution may or may not take place, hemoconcentration does not.

In burn injury, there is a very considerable loss of fluid and a large amount of edema in the burned area, as well as a very great loss of fluid to the exterior. An extreme indication of its magnitude is the observation of a loss of 10 liters over a 24 hour period in a 70 % burn of the body surface.

Anemic anoxia. In the anemic form of oxygen lack there is a decrease in the amount of circulating hemoglobin which can be differentiated from the anoxia of hemorrhage. In hemorrhage there is a decrease in the absolute amount of hemoglobin present and a decreased blood volume. In anemic anoxia, the blood volume is within the normal range, but there is a decrease in the concentration and in the absolute amount of hemoglobin. The consequent respiratory stimulation increases the respiratory exchange. There is an increase in cardiac output and an attempt to increase the blood flow to the tissues making up for the decrease in the oxygen-carrying power of the blood. This seems to be associated with the decrease in the viscosity of the blood which is present under these circumstances.

One can have a normal amount of hemoglobin present with a certain amount of it non-functioning, as when a gas, such as carbon monoxide in low concentration, has been inhaled. The carbon monoxide is absorbed in the lungs just as oxygen is, and it hooks on to the same part of the hemoglobin radical which ordinarily is combined with oxygen. Since carbon monoxide combines with hemoglobin, there is an affinity of between 200 and 300 times that of oxygen. Only a very small amount of carbon monoxide need be present in order to combine with rather large amounts of hemoglobin. Under these circumstances there is a decrease in the amount of functioning hemoglobin, i.e., the amount of hemoglobin available for combination with oxygen; therefore, the oxygen-carrying power of the blood is decreased.

It is important to realize that carbon monoxide is a much more dangerous form of anoxia than is anemia. Haldane many years ago pointed out that with a loss of 50 % of hemoglobin in the body and the blood volume maintained, one may show very few symptoms under conditions of rest. However, when 50 % of the hemoglobin is combined with carbon monoxide, the individual is almost helpless, because when carbon monoxide combines with hemoglobin it becomes very difficult for the hemoglobin to release the oxygen with which it is also combined. Tissues therefore suffer from very much more serious anoxia.

Histotoxic anoxia. This is a defect in the oxidative processes which take place in the tissues. A classic example is cyanide poisoning. The tissue enzymes are poisoned to an extent where the tissues cannot consume oxygen; there is no defect in the oxygenation of the blood nor in the blood flow. How acute the poisoning may be depends upon the concentration that is breathed. When very high concentrations are breathed, death is almost instantaneous; when very low concentrations are breathed the poisoning may not be lethal for some time. Under these circumstances, anoxia with the classic clinical symptoms occurs and death takes place some time later. (Walter Root, in The Hazard of Asphyxia in National Defense: A Symposium, 12 June 1951)

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Clinical Evaluation of Vergitryl, a New Highly Purified Extract of
Veratrum Viride

The availability of a highly purified, well-standardized preparation of *Veratrum viride* (Vergitryl) in both parenteral and oral forms suggested an evaluation of this agent. Vergitryl by the oral route of administration has been used in the treatment of essential hypertension. In patients treated continuously for periods of 6 months to more than 1 year the drug appears to be at least as effective and no more toxic than other available *Veratrum* preparations.

In this paper, the authors report on the use of Vergitryl in the management of toxemias of pregnancy. Various reports have appeared concerning the beneficial effects of *Veratrum viride* in the hypertensive toxemias of pregnancy. However, the use of crude extracts did not permit standardization of dosages, and undesirable side-effects were frequent. The purpose of this report is to call attention to the apparently greater predictability of response and the diminished incidence of major side-effects when the purified preparation is used.

Preliminary observations indicated that the majority (95 %) of toxemic patients exhibit a definite fall in blood pressure with minimal or no side-effects following an intramuscular dose of 0.75 unit of Vergitryl. This circumvents the technically difficult and time-consuming procedure of titrating each patient separately as is necessary in the technic of continuous intravenous administration of the crude extracts. Therefore, all nonconvulsive patients were given this dosage initially. The drug was mixed with 1 cc. of 1 % procaine in order to prevent local pain. Recent evidence with the use of other local anesthetics suggests that procaine also inhibits the development of nausea and vomiting. The blood pressure and pulse rate were recorded every half hour, and whenever the blood pressure rose above 140/90 mm. Hg. the dosage was repeated, thus permitting the adoption of a routine dosage schedule. In the occasional case in which no decrease in arterial pressure occurred 1 hour after the initial dose of 0.75 unit (0.05 cc.) of Vergitryl, it was increased to 0.9 unit (0.6 cc.), and if necessary at the end of an additional hour to 1.05 units (0.7 cc.) until an effective dosage was obtained. If nausea or vomiting occurred it was treated immediately with 50 mg. of pentobarbital sodium given intravenously.

In 17 cases of moderate to severe preeclampsia the hypertension and symptoms of toxemia were quickly controlled following the use of Vergitryl. In cases of mild preeclampsia similar results were obtained. Of 15 patients who had a past history of essential hypertension and a superimposed toxemia, 13 exhibited reduction of blood pressure to 140/90 mm. Hg. or less and clearing of signs and symptoms. Of 46 patients who exhibited elevation of blood pressure in the early postpartum period (so-called postpartum preeclampsia), 44 responded promptly to the use of Vergitryl with reductions of arterial pressure to the normal range.

It was apparent, therefore, that Vergitryl, usually given in a standard dose of 0.75 unit intramuscularly, produced a prompt fall in arterial pressure to the normal range with accompanying clinical improvement as manifested by subsidence of edema, albuminuria and retinal angiospasm in the majority of cases

of nonconvulsive toxemias. Repeated doses of the drug could be given as often as once per hour when necessary to maintain the hypotensive effect, although the usual interval between doses was 3 to 4 hours. Severe toxic reactions were not seen, and nausea and vomiting occurred in only 11 % of the cases. There were no cases of maternal or fetal mortality in the series.

In the convulsive or eclamptic toxemias the intravenous route of administration was utilized in order to obtain an immediate effect. In 8 patients so treated the convulsions were promptly controlled, and the blood pressure was reduced in all cases. A living fetus was obtained in 7 cases. Moderate nausea and vomiting occurred in every case treated by the intravenous method but could be controlled by giving pentobarbital sodium intravenously. There was no maternal mortality.

The advantages of Vergitryl are seen, therefore, to be (1) predictable responses to standard dosages rather than individual titration of each patient, and (2) administration by the intramuscular rather than by the continuous intravenous route in all except the convulsive cases. (M. Ann. District of Columbia, Feb. 1952, F. A. Finnerty, Jr. & E. D. Freis)

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The Present Status of the Treatment of Toxic Goiter

This paper presents a brief summary of the various methods of treatment of toxic goiter that are available at the present time and the current attitude toward them.

Until a few years ago it was generally agreed that the best method of treatment was a subtotal thyroidectomy after adequate preoperative preparation with iodine, a high-caloric diet and rest. Various details had been perfected so much that the mortality from surgical procedures had dropped to about 1 % in leading clinics. In the past few years treatment has been greatly modified by the use of antithyroid drugs and radioactive iodine.

There are 5 methods of treatment available at the present time:

1. A subtotal thyroidectomy after adequate preoperative preparation with propylthiouracil, iodine and a high-caloric diet.
2. Medical management with antithyroid drugs.
3. Medical management with radioactive iodine.
4. Roentgen ray treatment of the thyroid.
5. Roentgen ray treatment of the pituitary.

The best method of treating toxic goiter in most instances is still a subtotal thyroidectomy after adequate preoperative preparation. When medical management is indicated, radioactive iodine appears to be preferable to antithyroid drugs. The most important use of antithyroid drugs appears to be in the preoperative preparation of patients who have the disease in severe form.

Radioactive iodine may be employed for medical treatment of exophthalmic goiter in patients over 55 years of age. It is also of value in the treatment of persistence and recurrence of exophthalmic goiter but it is uncertain whether it should be used for this purpose in younger individuals.

Sufficient time has not yet elapsed to be certain whether or not radioactive iodine causes carcinoma of the thyroid. Therefore, its routine use in the medical management of exophthalmic goiter at all ages is not warranted at present.

The consensus is that in most patients who have nodular goiter with hyperthyroidism the best method of treatment, regardless of the age, is a subtotal thyroidectomy after adequate preparation. Radioactive iodine is not as effective in the control of thyrotoxicosis in patients with nodular goiter as in those with exophthalmic goiter. (J. Clin. Endocrinol. & Metabol., Jan. 1952, W. O. Thompson)

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Recent Experiences With Influenza and Streptococcal Disease in a Recruit Training Center

In a large Naval recruit training center during January 1952 sick call visits at dispensaries rose rapidly week by week during the first 4 weeks. About 14 January, cases were diagnosed clinically as influenza for the first time. These cases appeared to be more severe than those in the 1951 outbreak, with high fever for 3 or more days followed by a long convalescence.

When patients were being hospitalized at a rate over 200 per day, on 28 January, 7 throat washings were taken for influenza virus isolations. On 30 January, 18 more throat washings and 36 throat cultures for streptococcus were done. The results of the latter were known by 1 February and showed 33 % positive for beta hemolytic streptococci. An epidemiology team was immediately sent in and on the 3rd and 4th established that 30 % of the personnel at the center harbored beta hemolytic streptococci. The entire training center population was put on chemoprophylaxis in accordance with recommendations of the Commission on Acute Respiratory Diseases and Commission on Streptococcal Diseases of the Armed Forces Epidemiological Board, which called for either 100,000 units of oral penicillin once daily or 1 Gm. of sulfadiazine once daily. The latter drug was to be used with the following precautions:

(1) Not more than 2 weeks at a time; (2) close bacteriological checks for development of resistant forms; (3) patients not to be treated with sulfa if they had been on sulfa prophylaxis.

On 5 February both drugs were started in selected groups with two types of control groups. Sick calls dropped from 630 on the day the drugs were started to an average of 370 per day by the 4th day of the prophylaxis regime, and continued thus for the next 5 days. The incidence has declined still further since 12 February.

The earliest typing of 3 strains of influenza virus recovered from throat washings of 28 January showed (February 11th) all three to be influenza A prime. Typing of 14 strains recovered from 18 later washings is not complete. Because of the advanced stage of development of the influenza outbreak at the time of its identification, vaccination was not considered practical. At about the same time, influenza B was recovered in cases at an Air Force activity in the Bay region of California.

This respiratory disease outbreak is of general interest because of the dissemination of influenza A prime and beta hemolytic streptococci which has probably been brought about by movements of trainees from the training center to receiving stations and elsewhere. The predominant type of streptococcus recovered here was type 12, followed by type 6 and type 3, respectively in that order. Typing has been attempted thus far only with 11 of the most common types, but 30 % of cultures have not typed out with this fairly broad screening method.

It is believed that acute streptococcal disease was brought rapidly under control, and the rheumatic fever complications thereby reduced through chemoprophylaxis. The carrier states may not be very much affected by the small doses used. In event of serious outbreaks of streptococcal sore throat elsewhere, permission may be requested for the use of chemoprophylaxis from the Bureau of Medicine and Surgery. (Preventive Med. Div., BuMed)

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Islet Cell Adenoma With Hyperinsulinism

Islet cell tumors of the pancreas are relatively rare. In 1927 Wilder and his associates confirmed the association of islet cell tumors and hyperinsulinism by the report of a malignant islet cell tumor which was found at operation in a physician with symptoms of insulin shock. The first successful surgical removal of an islet cell adenoma of the pancreas was performed by Graham in 1929. In this case there was immediate alleviation of all the patient's symptoms. Howard, Moss and Rhoads in a comprehensive review (1950) report that only 200 localized islet cell tumors of the pancreas, including both benign adenomas and suspiciously malignant tumors, have been surgically removed. In addition, 24 carcinomas of the islet cells were found at operation. Altogether, this review of the literature disclosed records of 398 patients with islet cell tumors including both those found at operation and those discovered during postmortem examination.

It should be emphasized that the state of spontaneous hypoglycemia is simply an indication of an alteration in the complex carbohydrate metabolism of the body rather than a clinical entity itself. Thus hypoglycemia may follow disturbances in the liver and in the thyroid, pituitary and adrenal glands, as well as resulting from exercise and dietary factors. These extrapancreatic causes must be considered in all cases in which organic hyperinsulinism is suspected.

Islet cell tumors occur most frequently in the tail and body of the pancreas, less often in the head. Although some tumors protrude from the surface of the pancreas, many are deeply situated in the substance of the gland. They are of a reddish lilac or purplish pink color, highly vascular, ranging in diameter from 0.4 to 2.0 cm., usually single but occasionally multiple. In most cases they are encapsulated and have a consistency which is firmer than that of the surrounding normal pancreatic tissue. Many of the tumors, although appearing grossly encapsulated, microscopically show invasion of the capsule.

Although the onset may be sudden, symptoms usually appear gradually over a period of weeks, months or years. The symptomatology of hyperinsulinism varies widely in its manifestations and is directly related to the effect of hypoglycemia upon the sympathetic and central nervous systems. Among those symptoms referable to the sympathetic nervous system are pallor, flushing, nausea, hunger, epigastric pain, dizziness, cardiac palpitation and syncope. Symptoms related to central nervous system disturbance usually occur for the most part in severe attacks and appear as slurring speech, diplopia, restlessness, tonic or clonic muscle spasms, convulsions and in extreme cases coma and death. Psychiatric manifestations, observed in all degrees of severity, include disorientation, retrograde amnesia, negativism, mania and apprehension. The chief diagnostic criterion is Whipple's triad, as follows: (1) attacks of insulin shock occurring during fasting or following severe mental or physical exercise (fatigue state), (2) blood sugar values below 50 mg. percent during attacks and (3) prompt recovery following the administration of glucose. In all patients exhibiting these features the presence of an islet cell tumor must be strongly considered until proved otherwise, provided careful study has been performed to exclude extrapancreatic factors, including liver diseases which alter glycogen storage and disorders associated with hypofunctioning of the anterior lobe of the pituitary, adrenal cortex and thyroid gland.

In a patient exhibiting the Whipple triad in whom extrapancreatic factors have been ruled out, surgery is indicated. Enucleation or resection is the procedure of choice when a tumor can be found either in the pancreas or in an heterotopic extrapancreatic location. If careful search fails to reveal any evidence of an adenoma of the pancreas, adequate subtotal resection of the pancreas is recommended. (Am. J. Surg., Jan. 1952, C. C. Blackwell)

* * * * *

Incidence of Tuberculin Reactors in a Series of 2,000 Patients Seen in a Private Practice of Internal Medicine

This is a study of the incidence of reactors to tuberculin in a series of 2,000 consecutive patients seen in the author's private practice of internal medicine.

The tuberculin test as an aid in the diagnosis of tuberculosis has become more useful, since the percentage of reactors has steadily decreased each year. In years past it was thought that the test was of little value in adults because practically all reacted, because in the early part of the century most adults had been infected with tubercle bacilli. As the drive to stamp out tuberculosis became more effective, the number of tuberculin reactors decreased so that now there are many adults who do not react. This enhances the usefulness of the test as a diagnostic procedure.

The technic used was the intradermal injection of 0.1 cc. of a 1:1,000 solution of old tuberculin provided by the Minnesota Department of Health. The intradermal injection produced a bleb which would sting immediately after administra-

tion. The test was read in 72 hours. A reaction is an area of edema or induration not less than 5 mm. in diameter. This was read by palpation. Suspected cases of tuberculosis who did not react to the first dose were given a second injection of 0.1 cc. of 1:100 solution of old tuberculin.

The best criterion of the effectiveness of tuberculosis control leading to the eventual eradication of the disease is found in the incidence of tuberculin reactors. In the United States, it is now estimated that definitely less than 50 % of the population would react to tuberculin if tested.

Among the author's 2,000 patients, the over-all incidence of reactors to tuberculin was 55.6 %. The incidence among the 1,221 females was 53.5 % and among the 779 males it was 58.9 %. Among persons from 20 to 89 years the average incidence was 59.9 %; and among those from 0 to 19 years it was 13.8 %. The younger the individual the less likely is he to be a reactor to tuberculin.

The tuberculin test is an important, single diagnostic procedure to discover those infected with tubercle bacilli. It is thought that there were a high number of tuberculin reactors in this group because many of these patients were being studied because of lung disease, and yet here the tuberculin test proved to be a most valuable rapid screening method to exclude the presence of tuberculosis. (Dis. of Chest., Feb. 1952, James Bellomo)

* * * * *

The Use of Temporary Polythene Shunts to Permit Occlusion, Resection, and Frozen Homologous Graft Replacement of Vital Vessel Segments

Not infrequently operative therapy for a wide variety of diseases affecting vital blood vessels is either not considered feasible; or, if proposed, is rejected as impracticable; or, if attempted, is abandoned as prolonged vessel occlusion or sacrifice is encountered. The authors report their experience with a method which, though imperfect, appears to have promise.

Two observations form the basis for this experiment: (1) the demonstrated practicability of homologous artery preservation and transplantation; and (2) the unhurried, accurate procedures which are now regularly employed in isolated aortic segments of patients with aortic coarctation and its attendant collateral circulation. In the absence of such a collateral circulation many patent vital arteries cannot be safely occluded long enough to permit careful dissection and grafting. Thus it appeared that an artificial temporary arterial shunt must be employed.

Like Clatworthy and Varco (1950), the present authors have used Polythene tubing for this purpose. The exact dimensions of the shunt required to maintain adequate minute-volume flow and pressure will be the subject of another report. In general a shunt to artery ratio of approximately 1 to 7 has been used. The number of shunts and their length, of course, depend on the configuration of the vessels to be occluded. The Polythene tubing may be inserted into an artery in diverse ways. Schafer and Hardin have had best results with the following technic:

First the tube is cut to proper length so that it curves well out of the operative field. The ends are then flanged by rotating the tube in an alcohol flame, after which the flange is manually molded in hot water so that it has the alignment and curvature of the vessel into which it is to be inserted. Two 000000 sutures are placed transversely in the presenting wall of the vessel proximal and distal to the point chosen for insertion. A longitudinal stab incision is made in the vessel between the sutures, the flanged end of the shunt is inserted into the defect, the ligatures tied, and the tubing withdrawn until the flange engages the vessel wall. A clamp is placed on the tube during insertion. With the proximal end in place this clamp is released and the shunt is allowed to fill with blood. The distal end of the shunt is placed, after which the clamp is again removed. The vessel then may be safely crossed-clamped for an indefinite period.

In both human beings and dogs it appears feasible to maintain adequate circulation via Polythene shunts during temporary occlusion of the aorta, thus permitting homologous graft replacement of resected aortic segments. Though not necessarily best for this purpose, frozen grafts appear to have yielded satisfactory results. This technic should be applicable to the management of a wide variety of diseases affecting vital vessels. The technic of obtaining the vessels, as well as the failures and successes with the method, are given in the original article. (Surgery, Feb. 1952, P. W. Schafer & C. A. Hardin)

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Operative Treatment of Flatfoot

Despite the fact that surgical shortening of the deltoid ligament has been done successfully for over 24 years and that this procedure was published in the Annals of Surgery in 1939, it has been overlooked by most of the textbooks. The rationale for this type of operation is that the cause of flaccid flatfoot is abnormal length of the deltoid, or medial ankle, ligament.

The author stresses the fallacy of making a more or less solid piece of masonry of the foot, as in arthrodesing operations. He believes that non-surgical, palliative measures relieve symptoms only, and rarely, if ever, effect a cure in the anatomical sense. While the decision for surgical or palliative treatment must remain a matter for the judgment of the surgeon, if anatomical restoration to the normal is desired, the decision for surgery will not long be delayed.

This article does not deal with the rigid flatfoot with complicating arthritis nor with the traumatic flatfoot with skeletal deformity resulting from poorly treated fractures in the vicinity of the ankle. Likewise this operation is not indicated in the deformity resulting from poliomyelitis.

The mechanics of the common flaccid variety of flatfoot, is based on two premises: (1) the position of the heel bone (calcaneus) is the key to the deformity; (2) the heel bone is held in its correct vertical attitude by a deltoid ligament of normal length.

Surgical shortening of the deltoid ligament was suggested by the procedures of Nové-Josserand and Ober for the correction of congenital equinovarus, it having been properly reasoned that if surgical elongation of the deltoid ligament would correct varus, its shortening would correct valgus deformity.

Technic of Operation. The operative technic is simple. The incision begins behind the medial malleolus and ranges forward and around that bone to curve forward to the talonavicular joint; this allows adequate exposure when the skin is dissected upward. A flap of periosteum is raised from the exposed malleolus, and this subperiosteal dissection is extended distally to free the deltoid ligament down to its fan-shaped insertion on the talus behind, the sustentaculum below, and the navicular in front. It is further freed along its anterior border by incision of the soft parts between the distal anterior angle of the malleolus and the navicular, it being preferable to do this in advance of the deep separation of the deltoid from the medial aspect of the talus. The foot is now brought into a position of forced inversion or varus with special attention to the heel. The periosteal-ligamentous flap is next drawn tautly upward and excised to the extent that it now overlaps the periosteal edge above, and thus its redundant length is removed. The ligament and periosteum are now closed with chromic catgut or kangaroo tendon, and it is well to place two mattress stay sutures through the deltoid ligament and attach them above as an aid in holding the flap taut during closure. One should avoid opening the tendon sheaths behind and below the malleolus during dissection. In clearing the ligament from beneath the malleolus, it is well to dispose the periosteal elevator in a vertical direction until the medial side of the talus is reached. The foot is fixed firmly in marked inversion or varus in plaster of paris, always with emphasis on the heel. The tendo achillis is elongated if indicated.

The after-care is extremely important. No weight-bearing is allowed for at least a month. It is equally imperative that no unsupported walking be done for 6 months, which means that the heel varus must be protected at all times for that period by the constant use of shoes or slippers with their heels raised on the medial sides or flatfoot braces which accomplish the same purpose. At the outset of weight-bearing, the continuous heel varus may be materially assisted by the use of adhesive strapping. There must be no barefoot walking or standing during the 6 months of convalescence and the use of soft shoes is strictly interdicted. Neglect of these precautions will almost certainly result in a partial recurrence of the deformity or worse.

The operation has been done on patients from early childhood to the late thirties with equally good results. However, patients under 5 years of age are not the best subjects because of the greater difficulty of separation of the ligament from the softer bones of that period. Among clinic patients, the subsequent development of arthritis in consequence of latent neisserian infection has been noted in a few adults with disastrous results.

The author emphasizes that the operation has, in his hands, been entirely adequate and free from the inevitable consequences of stiffness and inelasticity of the joint-destroying operations. (Surg., Gynec. & Obst., Feb. 1951, B. L. Schoelfield)

Follow-Up Studies Following Total Pelvic Viscerectomy

It is becoming apparent that total pelvic viscerectomy with uretero-intestinal anastomosis is a feasible operative procedure for certain pelvic neoplasms. Though the operation is severe and the mortality rate considerable, the procedure affords certain patients palliation and the possibility of "cure" in circumstances which would have been considered hopeless a few years ago.

This presentation covers an experience with the radical operation, that is, total removal of pelvic viscera and pelvic lymph nodes en bloc. Partial viscerectomies have been carried out for many years, and they and radical Wertheim operations are not considered in this report.

The total viscerectomy as now carried out consists in either abdominal-perineal or supralelevator resection with terminal sigmoid colostomy and anastomosis of ureters to colon. Usually the right ureter is anastomosed to cecum or ascending colon and the left ureter is anastomosed to sigmoid colon. A simple nontunneled, end-to-side uretero-intestinal anastomosis is utilized. As in most instances the pelvic peritoneum is widely sacrificed, pelvic reperitonealization is usually not possible, and it is probably unnecessary. The operation ordinarily lasts from 2 to 3 hours, and on the average 3,000 cc. of transfused blood is required. Intra-arterial transfusion has been of unusual benefit in instances in which it has been employed because of rapid and severe bleeding during operation. Consideration is being given to employing it as a routine technic in operations of this type. Early in the operation the hypogastric arteries are ligated to minimize blood loss and the hypogastric veins are ligated both to lessen venous bleeding and to reduce the incidence of postoperative pulmonary embolism.

Total pelvic viscerectomy has been carried out by the author in 27 patients during the past 4 years. Sixteen patients had locally extensive rectal or rectosigmoid cancers, and 10 patients had cancer of the cervix, recurrent after irradiation therapy. In one patient there was an unusual extension of prostatic cancer to bladder and rectum which required this procedure. It is of interest that in 5 instances of extensive carcinoma of the ovary or of the body of the uterus none was removable by total pelvic viscerectomy. If such cancers were sufficiently invasive locally to justify the operation, there was invariably spread beyond the field of operability. During this 4-year period exploration was carried out in about an equal number of patients with the intention of performing total pelvic viscerectomy, but they were not subjected to the operation because of extension of the neoplasm beyond the limits of the pelvis. The author believes that the procedure should not be carried out unless it will remove all gross carcinoma.

Eight patients died within 1 month after operation, giving an operative mortality rate of 30 %. There were no deaths on the operating table.

Nine patients died 1 to 18 months after operation and are considered to have had short-term survivals. Three of these 9 patients were completely restored to normal health and activity for many months before death, and in them the operation afforded real palliation and prolongation of life.

At this writing, 10 patients are living and well from 2 to 48 months after operation. Four of them represent survivals of more than 30 months after operation.

The patients who survive the operation are generally freed of pain and lead normal lives despite the "wet colostomy" which requires the use of a "glue-on," ileostomy-type bag. In general the renal complications are not excessive, and in only 1 patient who survived the operation has there been a tendency toward chronic acidosis. Patients who recover from the operation only to die many months later of recurrence and metastasis have good palliative relief and lead essentially normal lives up to a final period of rapid deterioration.

From the results in this series it would seem that the operation of total pelvic viscerectomy is of real value to patients with certain extensive pelvic cancers, affording definite palliation for many patients and the possibility of "cure" for some. (A. M. A. Arch. Surg., Feb. 1952, E. S. Brintnall)

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Ehlers-Danlos Syndrome

The syndrome of hyperelastic skin associated with orthopedic abnormalities has been described many times, and there are readily available summaries of the literature written both before the description of this syndrome by Ehlers and Danlos and more recently. The present paper suggests a possible relationship between hyperadrenocorticism and this disease.

While hyperelasticity of the skin (dermatochalasis), extreme flexibility of the joints (arthrochalasis), and the formation of pseudotumors and subcutaneous nodules are usual features of the completely developed Ehlers-Danlos syndrome, it is commonly agreed that one of the most striking manifestations is extreme fragility of the skin (dermatorrhesis). Moreover, these patients experience great difficulty in healing even the smallest cuts and bruises. There is a marked absence or delay of fibrous tissue formation, so that eventually the wound is covered by epithelium, giving rise to the fragile, papyrus-like scars described by various authors.

The abnormality of the subepithelial structure is emphasized by recent histological studies. In many of the older reports the sections were reported as showing an overabundance of elastic fibers, although some found no such prominence of the elastic tissue. On the other hand, more recent histological studies have indicated that the basic pathological changes may be in the collagen substance.

In addition to the striking abnormalities of the cutis and subcutis, these patients often exhibit a remarkable fragility of the blood vessels, so that even gentle handling may result in marked ecchymosis and purpura. Some authors, in trying to explain the vascular fragility, found a low ascorbic acid content of the blood, with increased retention of the vitamin after administration of a test dose.

The symptoms referable to the skin and blood vessels of patients with Ehlers-Danlos syndrome seem to bear considerable resemblance to the findings in patients suffering from Cushing's syndrome or receiving prolonged treatment with ACTH. It is generally known that corticotropin and cortisone exert profound effects on the collagen system. Retardation of healing in patients with Cushing's syndrome has been reported by Cope, who in recent years has operated on most of these patients at the Massachusetts General Hospital, Boston. It is also well established that there is a failure of, or a delay in, the granulation of wounds suffered by patients under treatment with corticotropin or cortisone. This has been reported in human subjects and has been experimentally demonstrated in rabbits. Moreover, Ragan and associates, impressed by the fragility of the blood vessels, with consequent tendency to bruising and ecchymosis, were able to demonstrate a low blood ascorbic acid and a decreased urinary excretion of vitamin C in both human and animal subjects who were receiving prolonged treatment with corticotropin.

The patient whose case history is presented was studied with these facts in mind. A 4 1/2 year old white boy had the following symptoms, signs and laboratory findings which may also be observed in patients with adrenal hyperadrenocorticism: dermatorrhesis, poor fibroblast response to subcutaneous injury, fragile blood vessels, weakness, osteoporosis, delayed epiphyseal development, high normal or slightly increased excretion of 17-ketosteroids in the urine, increase of the uric acid to creatinine ratio in the blood and eosinopenia. (A. M. A. Am. J. Dis. Child., Feb. 1952, Abram Kanof)

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Asthmatic Dyspnea

One distinguishing characteristic of asthmatic dyspnea, in the typical case, is its tendency to occur in attacks. These come on any time of the day or night, commonly however at night, especially after midnight or toward early morning. The duration of the attacks varies from one to several hours. If a patient says his shortness of breath lasts only 5 to 10 minutes, it is not likely to be asthmatic in origin. In the uncomplicated case, there is no discomfort between the attacks. When the asthmatic spell has subsided, the patient is able to work and exert himself physically without bringing on any dyspnea.

A consideration of factors which precipitate asthmatic dyspnea helps to distinguish it from other types. First and most important is exposure of the individual to allergens to which he is sensitive. Second, respiratory infections often will set off an asthmatic attack. Then there are other factors such as laughing, coughing, emotional shock, eating cold food and drinking cold beverages, and inhaling cold air, strong odors, irritating fumes and particulate matter such as smoke.

Attacks of asthmatic dyspnea come on suddenly, regardless of what the patient is doing. He may get an attack if he is lying down, sitting, standing or while up and about. They usually attain their maximal severity within a few

minutes. During the attack, patients prefer to sit up in a chair and if possible to rest their elbows on a table. They may assume grotesque positions by which they bring their accessory muscles of respiration into play and thereby obtain as much air as possible.

Asthmatic dyspnea is obstructive in type. Excessive secretion of mucus by the bronchial mucosa and bronchospasm are responsible for the bronchial obstruction which leads to the dyspnea of the asthmatic attack. This dyspnea is more noticeable on expiration than on inspiration. The explanation of this, at least in part, is the greater bronchial obstruction caused by the anteroposterior collapse of the trachea during expiration.

The symptoms associated with asthmatic dyspnea help to distinguish it from other types. First of all is wheezing. This is a highpitched, whistling sound, loud enough at times to be heard across a room with the unaided ear. On the other hand, if the attack is severe and there is marked bronchospasm, the wheezing may be so high pitched that it can hardly be heard even with careful auscultation.

Coughing is another symptom associated with asthmatic dyspnea. This may be paroxysmal or almost incessant. Early in the attack, it is dry and non-productive but as the attack tends to subside, it becomes productive easily of appreciable amounts of sputum. Unless the patient has chronic asthma of long duration, there is no coughing between attacks.

Expectoration of sputum is another feature associated with the asthmatic attack. Typically the sputum is white, thick, gelatinous and tenacious. When examined microscopically it is found to contain many eosinophils and may also contain Curschmann's spirals and Charcot-Leyden crystals. If blood is present in the sputum, it may indicate an associated obstructing lesion of a bronchus such as carcinoma or bronchostenosis. Two other associated symptoms are cyanosis and sweating. These are seen with asthmatic dyspnea only if it is severe to extreme.

Finally, characteristic of asthmatic dyspnea is the almost invariable and remarkable relief which a small subcutaneous injection of epinephrine affords. Epinephrine is likewise effective by inhalation. Other drugs which relieve asthmatic dyspnea include ephedrine and its derivatives given orally and aminophylline administered either orally, rectally or intravenously. Rest does not relieve an attack of asthmatic dyspnea. (Proc. Staff Meet., Mayo Clin., 30 Jan. 1952, G. A. Koelsche)

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Psittacosis

Psittacosis (ornithosis) is a highly infectious disease caused by a filtrable virus which is endemic in birds and is readily transmissible to man. Most infections in man are acquired from members of the parrot family. Chickens, pigeons, fulmars or petrels, and canaries have also frequently transmitted the disease to man. However, since psittacosis is acquired by droplets from nasal

secretions, as well as by handling dead or sick birds or their cages, there have been human case-to-case infections recorded.

The incubation period of psittacosis is 7 to 15 days. The initial symptoms are fever, malaise, headache and anorexia. The temperature is usually remittent and remains elevated for 2 to 3 weeks. There is a nonproductive cough and x-ray evidence of a patchy consolidation beginning at the hilum, but usually no physical signs of pneumonia. The leukocyte count and respiratory rate remain normal and the pulse remains slow in relation to the temperature. Before the development of aureomycin and terramycin the mortality rate was about 20 %. Now it is considerably lower.

Five adults spent several hours on 27 May 1951, visiting a parakeet aviary. The owners of the aviary were convalescing from an illness that had been diagnosed as virus pneumonia. The two younger members of the group did not become ill, but the 3 older members of the group were all ill on 7 June.

One of the group became quite ill, was hospitalized and developed a typical case of psittacosis which was verified by positive complement fixation tests in increasing titers.

The other 2 patients were ambulatory and their illness would not have been diagnosed as mild cases of psittacosis had not the previous case been diagnosed and the common exposure to parakeets determined. They, too, had positive complement fixation tests to psittacosis antigen.

Two of the patients¹ were treated with terramycin. Although there are several reported cases treated with aureomycin and chloromycetin, no other cases have been found reported in American or English literature which have been treated with terramycin. The role that terramycin played in the recovery of these patients is difficult to determine as they had been ill for 2 weeks before the disease was diagnosed and terramycin started. However, the rapid deferescence of 1 patient and the symptomatic improvement in both cases in which it was used leads one to believe that terramycin played a definite part in their improvement. (J. Indiana M. A., Feb. 1952, M. A. Bassett)

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Pemphigus Vulgaris

The differentiation of pemphigus vulgaris from the two bullous diseases resembling it most closely, dermatitis herpetiformis and erythema bullosum, is important from at least two viewpoints. First is that of prognosis, a fatal outcome being expected in pemphigus vulgaris. Second is that of drawing conclusions from the responses to therapeutic trials of antibiotics and hormones, such as ACTH and the adrenal steroids. Obviously, a therapeutic success has entirely different and greater significance when there is certainty that the condition under treatment is definitely pemphigus and not another bullous disease resembling pemphigus.

Pemphigus vulgaris, excluding definitive pemphigus vegetans and foliaceus, is a bullous disease with the following clinical features: (1) It is invariably fatal

so far as can be judged at present, with a possible reservation concerning the efficacy of corticotropin and cortisone therapy in some cases. (2) The duration of the disease in the large majority of patients is under 1 year, although in a minority it may be more than 3 years, continuously or with remissions. (3) Lesions of the mucosae appear initially and/or throughout the course of the disease in the vast majority of patients. (4) Itching is not an important or prominent symptom. (5) The disease seldom occurs in persons under 30 years old.

The bulla is characteristically intraepidermal, but this location is not pathognomonic. The primary change is acantholysis or cleavage of the epidermis at, or close to, the suprabasal level, and there is extension into the rete pegs, the appendages, peripheral, and adjacent epidermis. Epidermal cells are liberated into the cavity of the bulla, singly or in clumps. The inflammatory reaction is secondary, variable and not characteristic. The processes of erosion and repair can confuse the primary intraepidermal site and structure; nevertheless, enough of the primary features may persist to be of diagnostic aid.

The histologic appearance of the bulla, in conjunction with the clinical picture, is at present the most reliable means of differentiating pemphigus vulgaris from the similar major bullous diseases, dermatitis herpetiformis and erythema multiforme bullosum. (A. M. A. Arch. Dermat. & Syph., Feb. 1952, William Director)

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The Incidence, Distribution and Significance of Megakaryocytes in Normal and Diseased Human Tissues

This study was done in response to the need for basic information regarding the sites and distribution of the megakaryocyte in human tissue, both normal and diseased.

There is a lack of such information, even though the megakaryocyte has been recognized as a distinct component of the bone marrow since 1890. Soon thereafter this giant cell was discovered in the capillaries of the lungs and in the circulating blood. Although the thrombocytopoietic role of the megakaryocyte and its relationship to bleeding and to thrombosis is almost universally accepted, there is still need for information regarding the normal origin and residence of the cell, the mechanism of thrombocyte production and the significance of circulating megakaryocytes.

Numerous megakaryocytes may appear in the circulation in blood dyscrasias of various types. Certain observers have demonstrated the increase in megakaryocytes in sections of bone marrow of patients dying of infectious disease, especially pneumonia. In sections of bone marrow in idiopathic thrombocytopenic purpura Nickerson and Sunderland noted a preponderance of "functionally active" forms and a decrease of degenerating forms of megakaryocytes, the total numbers being widely variable. They regarded the presence of megakaryocytes in the sinuses of the spleen and in the vessels of other organs as a

characteristic finding in idiopathic thrombocytopenic purpura. Hertzog also noted megakaryocytes in the spleen but did not consider as more significant. The increase in megakaryocytes, especially the young forms, in the bone marrow in his study of 36 cases of essential thrombocytopenic purpura. This is in agreement with the findings of most observers including Dameshek and Miller who noted an increase in megakaryocytes in aspirated marrow studied by various technics.

It is probable that determination of the megakaryocyte content of the bone marrow can be done most accurately by means of histologic section of tissue sufficient to allow evaluation of 100 "high power fields." Examination of the bone marrow sections yields reliable results. It is unfortunate that there is lack of correlation of results obtained by the several methods, i.e., examination of stained "smears," of sections of marrow and of cell counts performed by using a hemocytometer.

In a recent study, Brill and Halpern demonstrated megakaryocytes in sections of the lungs in all of their 50 autopsied cases and in the spleen of about two-thirds of these cases. They noted that an increase in megakaryocytes in the lungs was roughly related to the simultaneous occurrence of these cells in the various organs. They stated that "under normal conditions megakaryocytes in small numbers circulate in the blood stream," although their series did not include normal individuals. The material of the present authors includes essentially normal human tissues from cases of traumatic and other types of "sudden death."

The present study was designed (1) to determine the incidence of megakaryocytes in "routine" histologic sections of normal human bone marrow and of normal human organs; (2) to determine the incidence of megakaryocytes in "routine" histologic sections of bone marrow and organs of ill persons dying of various types of disease and (3) to attempt to correlate any variations noted with the type of disease.

According to the authors, their data do not contain any significant evidence toward proving the site or the sites of origin of the megakaryocytes. However, they state that not once did they observe a megakaryocyte attached to and apparently arising from the lining of a vascular channel.

The fairly old observation of circulating megakaryocytes has again been corroborated. Some quantitative information is presented in the complete article. Of significance is the repeated demonstration of megakaryocytes in the capillaries of the majority of cases of "sudden" death, whether of traumatic or natural cause. However, most of these circulating megakaryocytes were effete forms as represented by enormous nuclei with scant or no cytoplasm. Observation of these cells in "normal" individuals confirms the conjectures of previous authors who believed that megakaryocytes circulate normally in the blood.

The increased number and wide distribution of megakaryocytes in the tissues of ill persons is probably due to abnormal liberation of bone marrow elements during periods of stress. The phenomenon is probably analogous to or part of a leukemoid reaction and may well be an expression of the agonal state. The spleen and lungs nearly always show megakaryocytes in both normal or diseased persons but this does not necessarily mean that either of these tissues

generates these cells. The low blood pressure and wide vascular bed in the lungs is conducive to loitering of cells in the pulmonary circulation. The spleen is well known for its filtrative functions. However, well preserved, apparently normal megakaryocytes were found more frequently in spleen than in the lung. Further, their not uncommon interstitial location in the spleen suggests origin there, as well as in the bone marrow.

The demonstration of megakaryocytes in other organs is more difficult and the mechanism for trapping the cells is less obvious, except for the kidney. A megakaryocyte encountered in the kidney is almost invariably found in a glomerulus, suggesting that the cell was arrested during a phase of ischemia and rest for that particular glomerulus. In other organs of the body, the demonstration of a megakaryocyte depends to a greater degree upon diligence and chance.

The bone marrow displays megakaryocytosis when stimulated by infection or by almost any disease in general. Pneumonia as a stimulus to proliferation of bone marrow elements including megakaryocytes has been noted previously, and this finding is confirmed by the present data in which infection caused an average increase of megakaryocytes in the marrow of almost 50 % (i.e., 2,970 increased to 4,470). Although diseased persons in general present high counts of these cells in the bone marrow, there is considerable individual variation among diseases and with aging of the patient.

Patients with cirrhosis tend to have a low content of megakaryocytes in the marrow, according to the authors' results, which are in disagreement with previous studies which found normal or increased megakaryocytogenesis. However, the determinations of earlier authors were made upon aspirated sternal marrow, a method which may be inadequate for precise quantitative study.

Age is well recognized as an important factor in the structure and function of the bone marrow. Study of the cases of "sudden death" makes it apparent that the megakaryocyte content of "normal" bone marrow decreases with increase in age. This parallels the decrease in general cellularity of the marrow which has been recognized as a manifestation of aging. Smith and Butcher's average normal of 2,970 megakaryocytes per cu. mm. of bone marrow among their 36 control cases is somewhat below that found by Williams who studied 16 "control" cases of traumatic death (ages 19 to 70 years). He established his upper limit of normal as 5,000 megakaryocytes per cu. mm. of marrow.

Determinations of the percentage increase in megakaryocytes in the bone marrow with illness shows no significant difference among the various age groups. A trend is indicated by the great difference between the normal and the ill of the earlier decade. However, statistical analysis (including data from all individuals in both ill and well series) shows that this apparently exaggerated response is probably not significant. (Blood, Feb. 1952, E. B. Smith & J. Butcher)

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Placental Serum Therapy for Rheumatoid Arthritis

In the treatment of rheumatoid arthritis, ACTH and cortisone have some definite drawbacks, in spite of the remarkable results obtained from them. These drawbacks are: toxicity, high cost and short duration of effects.

It has been known for some time that pregnancy has an ameliorating effect on rheumatoid arthritis. Barsi of England treated several patients suffering from rheumatoid arthritis with transfusions of blood taken from pregnant women. He reported excellent results, but these have not been confirmed in this country. Recently, Granirer used plasma obtained from postpartum women for the therapy of rheumatoid arthritis and reported good results. The difficulty lies in obtaining blood from postpartum patients.

Since the pregnant woman apparently develops substances which are of therapeutic value against rheumatoid arthritis and related diseases, it occurred to the authors that these substances might be present in the placental circulation. They began collecting blood, therefore, from the placenta and using the serum for the treatment of rheumatoid arthritis.

The authors treated 33 patients with active rheumatoid arthritis and 2 patients with Marie-Strumpell's disease, for periods varying from 3 months to 1 year. These patients were between 23 and 74 years; approximately 80 % were over age 45. Thirty of the 35 patients were women.

All the patients in this group had active rheumatoid arthritis. Criteria for activity were based on clinical findings (both objective and subjective), x-ray evidence of rheumatoid arthritis and an elevated sedimentation rate. Most of the patients had received previous therapy with gold, hormones, physiotherapy, salicylates or other drugs with either slight or no improvement. All were ambulatory.

The results were not so rapid or so spectacular as those reported with ACTH and cortisone. The degree and rapidity of improvement depended on the duration and the severity of the disease. The results were better in the more recent cases and in the younger age group. Definite, although slow, improvement did occur, however, in over 85 % of the patients. Beginning improvement followed the 4th or 5th injection and would continue 1 or 2 days. After the patients had received from 20 to 40 biweekly injections, the interval between injections could be lengthened to 1 week in about 1/4 of the patients. In 9 cases apparent clinical remissions were induced which lasted from 1 to 6 months. In those patients who then relapsed, retreatment again yielded good results.

There was moderate reduction of subjective stiffness and pain, pain on motion and articular tenderness in every case. Slight to moderate reduction of joint swelling, particularly of the proximal interphalangeal joints, occurred in 85 % to 90 % of the patients. There was a moderate increase of muscle strength and joint function, limited by destructive changes, in over 85 % of the cases. In addition almost all of the patients had an improved appetite, slept better and had an increased sense of well being. The elevated sedimentation rate was decreased in 25 % of the patients, but in none did it become normal. In this group of cases

there were no complete remissions and 4 unimproved cases.

For control observations, 2 different methods were used. One was to start a patient on pooled nonpregnant plasma and then substitute placental serum in the middle of the course of treatment. The other was to substitute non-pregnant plasma for placental serum in the middle of the course of treatment. With both methods there was improvement during therapy with the placental serum and absence of improvement with the non-pregnant plasma.

It is known that with many new methods of treatment for rheumatoid arthritis, a majority of patients will show an early temporary improvement. With the use of placental serum, however, it must be pointed out that a few weeks are required before any noticeable improvement occurs and the improvement usually continues only as long as semi-weekly injections are maintained.

Treatment must be continued over a long period of time in order to obtain the desired results. It is probable that substances in the placental serum other than ACTH or cortisone are responsible for the clinical improvement, since otherwise one would not expect the 1 to 6 months of apparent clinical remission which were obtained in 1/4 of the cases.

The good results are thought to be due to the effect of the placental serum itself. There were no untoward side effects or toxic manifestations in any of the patients.

The technic of obtaining placental serum is described in the original report. The serum is easily obtained and plentiful, costs little and has no untoward effects. (Am. J. M. Sci., Feb. 1952, W. Aronson, F. Levy, L. J. Besen & M. Leff)

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Vasa Previa

Vasa previa is one of the most unusual and tragic accidents in obstetrics. It is infrequently encountered, and yet undoubtedly more common than a review of the literature would indicate. In no other condition in obstetrics do we find so great a hazard for the infant and so little for the mother. In all the literature there is no report of a maternal death from this cause and yet the fetal mortality runs well over 50 % in those cases recorded. Despite the fact that the entity has been recognized for over 150 years, there has been virtually no improvement in fetal salvage.

Several conditions have been grouped together in the literature as vasa previa and these might better be separated into two groups. One is vasa previa, in which, by definition, the umbilical vessels present across the uterine os and act as a barrier, albeit a fragile one, to the presenting part. The vessels may rupture or not. It is, quite naturally, the rupture of the umbilical vessels which may result in a tragic outcome for the fetus. Since rupture of the vessels may occur even though the placenta is high and the vessels do not cross the os uteri, it seems logical to make a second group, abruption of the umbilical vessels. This latter classification would then include the cases of rupture of a shortened

umbilical cord or those in which the cord appeared normal and the condition of vasa previa did not exist.

According to von Franqué, and today his is the generally accepted theory, the abdominal pedicle ordinarily extends to the fetus from that portion of the chorion which is in contact with the most richly vascularized portion of the decidua. Usually this is the decidua basalis. In this way the cord becomes inserted upon the placenta. However, occasionally, during the first few days of pregnancy, the area of greatest vascularization may be in the capsular portion of the decidua and in such circumstances the abdominal pedicle takes its origin from that location. As the pregnancy progresses, however, the area of vascularization shifts to the basalis portion of the decidua - the actual site of the future placenta - while the abdominal pedicle retains its original position and from its maternal end the vessels extend to the margin of the placenta.

In those cases in which the placenta is situated in the lower uterine segment it is easily seen how a relatively innocuous-appearing velamentous insertion of the umbilical vessels can be of great practical importance. As the cervix dilates, the presenting part may be thrust against the abnormally situated vessels. If the membranes rupture, one or more of these vessels may be torn so that fetal blood loss occurs. Even if the vessels do not rupture they may be compressed against the bony pelvis by the presenting part and hypoxia of the infant occurs to such a degree as to cause his death. Occasionally the vessels have ruptured without the rupture of membranes or the exposed vessels may not rupture at all. Lefevre reported 5 such cases. The outcome in these cases, as might be expected, whether diagnosis was made prior to delivery or not, was a universally favorable one. It is possible for the aberrant vessels to lie above the lower uterine segment or even high in the fundus. In this situation, a long tear in the amniotic sac can extend into and damage vessels running between the chorion and amnion whether they cross the os uteri or not.

All treatment measures must of necessity be directed toward saving the life of the fetus, for at no time is the mother's life endangered. Once the diagnosis is made by palpation of the pulsating vessel in the cervix, the only treatment is the prompt delivery of the infant by the most available method. Spontaneous deliveries account for most of the cases in the literature, but one was by vaginal cesarean section, others by abdominal cesarean section, high forceps, low forceps, version and extraction, and by spontaneous and induced labors. There is apparently no real choice and the most available method of delivery has been that utilized. There is no doubt that once abruption of the umbilical vessels has occurred the infant must be delivered as rapidly as possible. He cannot tolerate even small blood loss in the presence of his normal mild intrauterine hypoxia. If the cervix is fully dilated and the fetus can be delivered from below that is the method of choice. Whether this be done by forceps application or version and extraction would depend on whether the other prerequisites for these methods of delivery exist. If the cervix is not fully dilated and labor has not progressed to a point that safe vaginal delivery can be achieved, a cesarean section should be done so long as fetal heart tones can be

heard. A cesarean section would not be justified in the absence of fetal heart tones or where blood loss has been heavy and heart tones are fading. (Am. J. Obst. & Gynec., Jan. 1952, W. E. Torrey, Jr.)

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Cost Consciousness

The personnel in governmental service are not likely to be as cost conscious as those in private enterprise because the operations in which they are employed are not predicated on profit but on providing a public service. Perhaps this lack in cost consciousness may be attributed to the stress that must be placed on performance, rather than on economy during periods of national emergency. Too, it may be assumed that some governmental personnel fail to appreciate fully that as taxpayers they will be called upon to help foot the bill for the operation of government in the form of taxes.

In the opinion of some strategists, the Kremlin's aim is victory by way of an economic war to bankrupt the United States, instead of an all out "firing" war. However, regardless of the type of war involved the conservation of resources (men, money and materials) is to be desired and encouraged strongly.

Cost consciousness must be developed as a frame of mind. It is necessary that an attitude, an awareness of the need for the economical utilization of personnel, material and fiscal resources, and example on the part of leaders at all levels, become second nature. In this way full value may be obtained for every dollar spent by the Medical Department.

Cost consciousness will soften the impact of our requirements upon an already heavily burdened national economy. (Comptroller Div., BuMed)

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Fourth Annual Navy Industrial Health Conference: Correction of Dates

In the Friday, 22 February 1952 issue of Medical News Letter (Vol. 19, No. 4), the Fourth Annual Navy Industrial Health Conference dates were given as 20 - 25 April. The Conference begins at 0900 Saturday, 19 April and goes through Thursday, 24 April. (Preventive Med. Div., BuMed)

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Current Morbidity - Highlights in Current Incidence

During November 1951 the morbidity incidence rate for all causes in the Navy and Marine Corps receded to 400.1 per 1,000. This is the lowest month thus far evaluated for 1951 and is slightly below the 426.9 per 1,000 during the corresponding month in 1950. Although the rate for injuries shows about twice as great a decrease as does that for disease conditions, both declined. Practically all disease conditions showed lower rates in November with the exception of infections of the digestive tract and some of the acute respiratory infections, including primary atypical pneumonia. The reduction in the incidence rate for accidents, violence and poisonings from 58.9 in October to 50.2 per 1,000 in November can be attributed mainly to the sharp decrease at noncontinental shorebased activities in the Pacific area, which reflects the lower incidence rate for non-disease conditions reported from the Far East. This may be owing to the lull in military activities in the Korean area during the truce negotiations.

Among those few conditions reflecting an increased incidence rate in November, were infections of the digestive tract, which includes such conditions as bacillary dysentery, amebiasis and dysentery, n.e.c. An outbreak of bacillary dysentery reported in the 6th Naval District accounted for a rise to 3.7 per 1,000 from 2.3 in October. The rate was also this high in July, when outbreaks of this condition were likewise reported.

The rate for infectious hepatitis of 2.8 per 1,000 maintains the higher level reached for this condition since the middle of the year. The incidence of malaria in the Navy and Marine Corps dropped sharply in November to 24 new cases as compared to the 104 reported in October. This is the first month that malaria has receded to less than 100 cases per month since the sharp rise which started in June 1951.

The incidence rate for inguinal hernia declined slightly in November to 4.7 from 5.0 per 1,000 in October. However, it is of interest that the rates for this condition reported from Marine Corps Recruit Depots, although declining slightly, are still much higher than the rates at Naval Training Centers.

Venereal disease shows a decline of better than 15 % in November with a rate of 37.8 per 1,000, and is lowest reported thus far during 1951. The November incidence rate is almost 40 % below the peak of 61.8 per 1,000 in January. (Statistics Navy Med., Feb. 1952)

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Training Course for Inactive Volunteer Naval Reserve Medical and Dental Officers in Amphibious Medicine

A training course in amphibious medicine of 2 weeks' duration for Naval Reserve medical and dental officers is to be conducted at the Amphibious Training Command, U. S. Naval Amphibious Base, Little Creek, Virginia. It is scheduled to convene on Monday, 7 April 1952 and continue to 19 April 1952.

The purpose of this course is to familiarize Inactive Volunteer Naval Reserve Medical Department officers in amphibious operations in general, and the medical aspects thereof in particular. The course consists of lectures, training films, demonstrations and practical exercises to familiarize Medical Department officers with the nature of the medical service provided in amphibious operations. The embarkation, underway and debarkation phases of the medical service are dealt with, and medical supply problems are presented.

Officers concerned should provide themselves with fatigue or utility-type uniform equipment for participation in the practical aspects of this course. Meals and sleeping quarters will be available at the Bachelor Officers' Quarters for those officers who desire such accommodations.

The 1st, 3d, 4th, 5th, 6th, 8th, 9th Naval Districts and the Potomac River Naval Command have been assigned quotas for this course.

Inactive Reserve Medical Department officers are encouraged to take advantage of the opportunity to attend this course on active training duty orders in a pay status. All inactive Volunteer Reserve Medical Department officers who desire to attend this course should submit their request to the Commandant of their home naval district at the earliest practicable date. (Reserve Div., BuMed)

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Change of Address

Please forward requests for change of addresses for the News Letter to: Commanding Officer, U. S. Navy Medical School, National Naval Medical Center, Bethesda 14, Maryland.

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List of Recent Reports Issued by Naval Medical Research Activity

U. S. Naval Medical Research Unit #3, Cairo, Egypt

Hypertonic Sodium Bicarbonate Infusion in Man - A Physiological Study With Clinical Implications, Project NM 007 082.02.01, 31 December 1951.

Medical Mission to Yemen, Southwest Arabia, 1951. II. A Cursory Survey of the Intestinal Protozoa and Helminth Parasites in the People of the Yemen, Project NM 005 050.39.20, 31 December 1951.

A Simple Technique for Following the Disappearance of Infused Colloidal Solutions, Project NM 007 082.01.03, 1 February 1952.

Blood Volume Estimation Following the Infusion of Non-Protein Colloidal Solutions, Project 007 082.01.06, 4 February 1952.

From the Note Book

1. CAPT John R. Poppen (MC) USN (Ret.), was honored on 28 January by the Institute of Aeronautical Sciences for his outstanding contributions to the advancement of aeronautics through medical research. He was presented the John Jeffries Award at the Honor Night Dinner of the Institute. He is the second naval medical officer so honored. Many consider CAPT Poppen's most significant contribution to the advancement of aeronautics through medical research to be his investigations and the resultant findings relative to the field of acceleration and its effect on pilots, which led directly to the development of the currently used G-suits by Naval aviators. (PIO, BuMed, 13 Feb. 1952).
2. Subcommittee 3 of the National Committee on Radiation Protection has voted that the recommendation published in Section 7.1d of National Bureau of Standards in Handbook 41 (Medical x-ray protection up to two million volts) be changed to, "The aluminum equivalent of the table top shall not be more than 1.0 mm. when measured at 80 kilovolts without a patient or phantom." NBS Handbook 41 is one of several x-ray protection codes prepared by the Committee and published by the National Bureau of Standards. (Tech. News Bull., NBS, Feb. 1952)
3. The BuMed Scientific Exhibit entitled, "U. S. Naval Dental Corps," was displayed at the 69th annual session of the Minnesota State Dental Association held 18-20 February 1952 at the St. Paul Hotel, St. Paul, Minnesota. The exhibit is designed in 6 individually constructed and self-contained units. By means of graphs, art work, models, photomicrographs and slides, it depicts the role of bacteriology in diagnoses of oral lesions, the value of rubber dam in airbrasive technic, partial denture design, endodontia, operative dentistry, crown and bridge work and occlusional equilibration. (PIO, BuMed, 13 Feb. 1952)
4. The methods of falling and of getting down and up from the floor in rehabilitation technics with braces and crutches are described in the American Journal of Physical Medicine, February 1952, by M. Hoberman and E. F. Cienia.
5. A urinalysis which uses adaptations of the direct-evaporation method is described. It provides a quick estimate of the possible seriousness of entry of radioactive substances into a worker's body during a contamination accident. (Nucleonics, Feb. 1952, F. P. Cowan & J. Weiss)
6. A conference on oxypolygelatin as a plasma extender was held at California Institute of Technology, February 4 and 5. Dr. Linus Pauling and Dr. Dan Campbell conducted the informal conference. Participants included ONR contractors associated with the plasma extender program, Oak Knoll Naval Hospital and Dr. Paul Lindsay, Head, Clinical Branch, ONR. (Clinical Branch, Bio Sciences Div., ONR)

7. "The Light Within the Darkness" is the title of an article appearing in the February 1952 issue of the Atlantic Monthly. This article is of interest because it is written by a practicing physician who is blind. The physician uses the pseudonym of Dr. Elliott Dobson.

8. A new group of chemicals effective in killing fungi on plants, such as late blight of tomatoes and late blight of celery, has been developed by scientists of the Shell Agricultural Laboratory at Modesto and Shell Development Co. at Emeryville, California. The chemicals are called alkyltetrahydropyrimidines. Preliminary tests in the laboratories and greenhouses indicate high fungistatic value. Results of these tests are reported in the journal Science, for 1 February. (Science News Letter, 9 Feb. 1952)

9. "Spinal Anesthesia for Vaginal Delivery With Special Reference to the Prevention of Postpartum Headache" appears in the American Journal of Obstetrics and Gynecology, January 1952. (CDR J. W. Huston, MC, USN & LT T. B. Lebherz, MC, USN)

10. A study of terramycin in the treatment of pulmonary tuberculosis appears in Diseases of the Chest, February 1952. (L. M. Pfefer, F. J. Hughes & W. E. Dye)

11. The University of Kansas has installed a color television system for under- and postgraduate medical instruction. Three direct-view receivers in as many rooms will accomodate audiences of up to 40 at each point. The sound system is two-way so that students may ask questions of the surgeon. (Science, 8 Feb. 1952)

12. The specificity of the L. E. cell in blood and bone marrow preparations, and its significance in the diagnosis and clinical concept of systemic lupus erythematosus is discussed in the British Journal of Dermatology, January 1952, by P. A. J. Smith.

13. A report of manifestations of toxicity resulting from the sawing and working of certain woods obtained from Spanish Guinea appears in Industrial Medicine and Surgery, February 1952. (J. Dantin-Gallego, A. F. Armayor, J. Riesco)

14. Dr. A. J. Chesley, Minnesota Health Officer, reports that 2 persons living in Minnesota developed psittacosis recently and that the probable source of infection was a parakeet which had been purchased in Florida by a young man and brought to Minnesota on January 6. One week later the bird developed diarrhea and ruffled feathers, and appeared ill. It died on 20 January and was destroyed. On January 16 the mother of the young man became ill and the father, 2 days later. X-ray examination of the mother's chest revealed a lesion in the right upper lobe and that of the father showed involvement of the left lower lobe.

Complement fixation tests were positive. Both patients recovered promptly following antibiotic therapy. These cases are the first from this source to be reported since it was discovered that several psittacine birds had died of this infection on a bird farm in Florida. (Communicable Dis. Summary, FSA, PHS, National Office of Vital Statistics)

15. Two Public Health Service officers, Emily Myrtle Smith and Genevieve Soller, are the first nurses assigned to Formosa and the Philippine Islands under the Mutual Security Agency program. Miss Smith will be stationed in Taipeh and Mrs. Soller in Manila. They will be chief nurse consultants to the MSA missions in these two capitals. The two nurses will work with Formosan and Filipino nurses and other health workers to establish and develop schools of nursing and to extend public health nursing in the two countries, particularly in the rural areas. (FSA, PHS, 21 Feb. 1952)

16. Dr. Roger D. Reid, Head, Microbiology Branch, ONR, and CAPT J.A.C. Gray, Research Division, BuMed, visited Duke University, the University of North Carolina and Camp Lejeune, 29 January - 1 February 1952. They attended meetings held for the purpose of establishing cooperation between the universities and Camp Lejeune on a project to be conducted at the latter activity concerning the origin of non-gonococcal urethritis. (Microbiology Br., BioSciences Div., ONR)

17. Dr. Benjamin Tenney, Jr., Professor of Obstetrics and Gynecology, Boston University School of Medicine, has accepted a position as Reserve Consultant to BuMed to represent his specialty. Doctor Tenney's acceptance of this position fills the vacancy created in this group by the death last year of Dr. Paul Titus. (PIO, BuMed, 20 Feb. 1952)

18. Officer and enlisted Naval Correspondence Courses are one of the most time-saving tools for increasing the training of men of the Organized Reserve. The more a Reservist learns at home through self-study, the more valuable he becomes to his organized unit and to the Naval Establishment as a whole. Correspondence courses also offer the opportunity for earning additional retirement and promotion points. They supply an open door to knowledge of training subjects beyond that which can be acquired through drill sessions. Through these courses both officer and enlisted man can find the book knowledge so essential to the background of a well-rounded Navyman. (U. S. Naval Correspondence Course Center, 4 Feb. 1952)

19. CDR George M. Lynch (MC) USN, Proctologist at the Naval Hospital, Oakland, California, recently became the first certified proctologist in the Navy Medical Corps. He was certified by the American Board of Proctology on 15 January, after taking his examinations in Philadelphia. (PIO, BuMed, 20 Feb. 1952)

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BUMED CIRCULAR LETTER 52-13

13 February 1952

From: Chief, Bureau of Medicine and Surgery
To: All Ships and Stations

Subj: Physical Examination, NAVMED-H-2; use of Standard Form 88 in lieu of

Ref: (a) Ch. 16 and Art. 15-82, ManMedDept

1. Effective immediately, the preparation of a form NAVMED-H-2 (Physical Examination) shall be discontinued, and Standard Form 88 (Report of Medical Examination) shall be prepared in lieu thereof. Instructions for the preparation and inclusion of the NAVMED-H-2 in the Health Record, contained in reference (a), shall apply to Standard Form 88 insofar as applicable.
2. Data currently entered on the reverse side of the NAVMED-H-2 terminating the Health Record, shall be entered immediately following the last entry on form NAVMED-H-8 (Medical History).
3. Present stock of form NAVMED-H-2 shall be destroyed.

H. L. Pugh

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BUMED CIRCULAR LETTER 52-14

20 February 1952

From: Chief, Bureau of Medicine and Surgery
To: All Ships and Stations

Subj: Preembarkation certificates and physical examinations for overseas travel of military dependents in MSTs vessels and MATS planes

Ref: (a) BuMed Cir. Ltr. No. 51-80; NDB Jan.-June 1951, 51-339, p. 94

Encl: (1) Preembarkation Certificate, DD Form 625

1. Enclosure (A) to reference (a) is hereby canceled. The Preembarkation Certificate, DD Form 625, enclosure (1) of this letter, shall be substituted therefor.
2. Current stocks of the old format may be used until the supply is exhausted. The new Preembarkation Certificate shall be reproduced locally.

H. L. Pugh

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NavMed-3889 . 3/52

PREEMBARKATION CERTIFICATE		Form Approved Budget Bureau No. 22-R101	
NAME (Print or Type) (Last) (First) (Middle)			
TO: The Medical Officer responsible for my care during travel			
NOTE: Check correct block; enter month of pregnancy if applicable; strike out phrase indicated by "*" if not applicable.			
I hereby certify that to the best of my judgment and knowledge I, <input type="checkbox"/> am not pregnant, <input type="checkbox"/> am pregnant in the ____ month of pregnancy, and I (and my children accompanying me, listed in "A" below)* have not had any illness or injury within 60 days except as indicated in "B" below.			
A. (List all children)			
First Name - Middle Name - Last Name		Sex	Age
B. (List below name of each individual and the illness or injury experienced within 60 days.)			
(Name)		(Illness or Injury)	
DATE:		SIGNATURE:	

DD Form 625
1 Feb 1952